

Opinion

Volume 7 Issue 4 - June 2018
DOI: 10.19080/CRDOJ.2018.07.555716

Curre Res Diabetes & Obes J

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Glucose Tolerance Test Applied in Screening of Anti-Diabetic Agent (S)



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Submission: May 26, 2018; **Published:** June 08, 2018

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Abstract

Oral glucose tolerance test (OGTT) is widely applied in the diagnosis of impaired glucose tolerance (IGT) and/or type-2 DM (T2DM) in clinical practice. Recently, it is also employed in the diagnosis of non-alcoholic fatty liver disease (NAFLD) and/or Non-Alcoholic Steatohepatitis (NASH) in patients without overt T2DM. In basic research, OGTT is also useful in the development of new agents for diabetic medication(s). However, it must concern the changes in basal glucose level showing at the 0min during OGTT. Therefore, the basal glucose level cannot be ignored and/or deleted in the evaluation of area under the curve (AUC) from plasma glucose disappearance curve during OGTT.

Keywords: Impaired glucose tolerance (IGT); Oral glucose tolerance test (OGTT); Clinical diagnosis; Diabetes; Fatty liver

Introduction

Functionally, blood glucose levels often elevate markedly after a meal and it is returned to the normal level through compensations. But, someone(s) fail to perform in a good way and they belong to hyperglycemia at a category which is abnormal but is still not reach the criteria of diabetes mellitus (DM) [1]. Then, they are classified as the impaired glucose tolerance [2]. In clinics, oral glucose tolerance test (OGTT) is widely applied for diagnosis of the impaired glucose tolerance (IGT) and/or type-2 DM (T2DM) while IGT is identified using the plasma glucose level between 140-200mg/dL during a 2-hour OGTT [2]. In the recent 10 years (2007-2017), there are 15,501 reports shown OGTT in MEDLINE/PUBMED while 66.6% of publications regarding the human studies. Generally, the shape of glucose curve during OGTT has been applied to reveal the risk of developing IGT [3,4] and the patterns of insulin concentration have also been used to predict the development of T2DM [5]. Moreover, the difference in time showing glucose peak has been suggested as an indicator of prediabetes and/or β -cell function [6].

However, the peak and decay in plasma glucose levels during the OGTT reflect the interplay between several factors, including the glucose intestinal absorption rate, insulin sensitivity, β -cell

function and components, such as β -cell glucose sensitivity, β -cell insulin sensitivity rate, and enhanced factor, in addition to the secretion of gut hormones. Therefore, application of OGTT in the diagnosis of IGT is useful but it seems limited in the study of the pathogenesis of T2DM without another indicator(s), as described in our previous report [7].

Recently, the prevalence of non-alcoholic fatty liver disease (NAFLD) is rapidly increasing around the world, similar to T2DM. Therefore, the association and/or relevance of T2DM, NAFLD, and glucose and insulin metabolism have been widely linked using OGTT in clinics. The postprandial insulin secretion pattern is associated with the histological severity in NAFLD patients without diabetes [8]. Interestingly, the risk of transient postprandial hypoglycemia in patients with NAFLD has been identified using OGTT [9]. Also, the value of glucose ≥ 155 mg/dL from a 1-hour OGTT has been used to identify a subset of non-glucose tolerant individuals at risk for NAFLD [10]. Moreover, Non-Alcoholic Steatohepatitis (NASH) has also been linked with T2DM, particularly a high prevalence of NASH in patients with T2DM more than 5 years [11]. Therefore, application of OGTT for diagnosis of NAFLD or NASH without overt T2DM is progressed to apply in the clinical practice, as described previously [7].

In basic research, OGTT used in animals is also mainly focusing on the glucose homeostasis. Insulin resistance (IR) and/or the insulin sensitivity have been identified using the results of glucose-insulin index obtaining from OGTT in animals [12]. Moreover, OGTT is also used to mimic the postprandial hyperglycemia, which may provide the data regarding the hypoglycemic effect as a consequence of changes in glucose utilization [13]. Generally, OGTT or meal tolerance test mimics the glucose and insulin dynamics under the physiological condition in animal studies. The postprandial rise in plasma insulin enables the disposal of blood glucose in the absorptive state, while the fall in plasma insulin contributes to keeping the glucose homeostasis in the post-absorptive state and/or during the starvation. Otherwise, the impaired glucose tolerance (IGT) is widely reflected in a larger incremental area under the curve (AUC) of the plasma glucose disappearance curve during OGTT. Results in OGTT shown a marked increase in $AUC_{0-120min}$ from the experimental group indicating the success of the diabetic model. Then, diabetic animals were used to screen with the investigated substance, either herbal extract or nutrient. Once the slope of the glucose disposal phase is markedly changed and AUC is more decreased than the vehicle-treated control, it means that the investigated substance has an ability to alleviate the impaired glucose tolerance, probably due to enhanced glucose utilization [14]. Therefore, OGTT is widely applied in the development of new substance(s) as the anti-diabetic agent using animal studies.

However, the fasting blood glucose was easily modified by the investigated substance and the basal glucose level in each group was not the same during OGTT [15]. Similarly, the basal glucose level is also significantly varied in mutant mice as compared to the wild-type littermates [10]. Then, it can be criticized that AUC is changed due to the difference in basal glucose level. Correction of the data in basal glucose level has been suggested in a review article [10]. In MEDLINE/PUBMED, there is 5187 paper shown OGTT in animals between 2007 and 2017. No one of them ignored the value of basal glucose level in the preparation of AUC during OGTT. It means the important role of basal glucose level showing at the 0 min during OGTT. Many factors could be considered in the maintaining of basal glucose level after drug treatment. Therefore, the real mechanism(s) for it shall be characterized in the future.

Conclusion

Oral glucose tolerance test (OGTT) is useful in the diagnosis of impaired glucose tolerance (IGT) in clinics. In basic research, OGTT is also useful in the development of new agent(s) for diabetic medication(s). However, it must concern the changes in basal glucose level showing at the 0 min during OGTT. The basal glucose level cannot be ignored and/or deleted in the preparation of AUC from OGTT.

Acknowledgement

We thank Miss Y.L. Yen for the kindly help in the collection of references.

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DOI: [10.19080/CRDOJ.2018.07.555716](https://doi.org/10.19080/CRDOJ.2018.07.555716)

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